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T-CELL LARGE GRANULAR LYMPHOCYTOSIS FOLLOWING AUTOLOGOUS STEM CELL TRANSPLANT

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T cell large granular lymphocytosis (T-LGL) following autologous stem cell transplant (ASCT) has not often been reported. There have been three publications referring to T-LGL developing after allogeneic SCT and one case report of a case of T-LGL leukemia occurring after ASCT. Here, we report four patients transplanted at our institution, who developed a clonal T-LGL following ASCT. The patients were transplanted for acute myeloid leukemia and non Hodgkins lymphoma with busulfan based conditioning regimens. One patient had myeloid and platelet non-engraftment two months post transplant, the others engrafted normally by D+28 but became mildly to moderately pancytopenic by day +100 without requiring transfusions. A peripheral blood smear showed increased numbers of large granular lymphocytes with phenotype CD2+, 3+, 8+, 57+ in upto 49% of lymphocyte gated cells. T cell gene rearrangement study was polyclonal for the beta chain by Southern Blot and monoclonal for the gamma chain by polymerase chain reaction in all these patients. A prolonged and aggressive disease course was noted in the one patient with delayed engraftment, with platelet transfusion dependency upto six months post transplant, but the others had an indolent course, and the pancytopenia gradually resolved in all four. Three of the four patients continue to be in remission 9-24 months post ASCT.

We contend that 1) clonal lymphocytosis, particularly T-LGL, following ASCT may not be an uncommon occurrence and may explain the observed post autologous transplant "slump" in counts in at least some instances, although other infectious etiologies should still be pursued. 2) In most patients this may be an indolent process that may be chronic or self-limited and does not seem to impair prognosis. 3) We suggest that a heightened awareness of this condition may be beneficial to explain pancytopenia following engraftment after ASCT and further attempts may be made to elucidate the etiology as well as establish the true incidence of this phenomenon.

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SINGLE-CENTER EXPERIENCE WITH THE EARLY USE OF AMD3100 PLUS G-CSF FOR MOBILIZATION OF HEMATOPOIETIC PROGENITOR CELLS IN PATIENTS CLASSIFIED AS POOR MOBILIZERS

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We report a single-center experience with AMD3100, the SDF-1α inhibitor, in patients treated after failing chemotherapy or growth factor based mobilization. Patients unable to collect ≥ 0.8 E6 CD34/kg in 2 days or 2.0 E6 in 4 days (7, 25%) or unable to achieve absolute PB CD34/uL ≥ 15 and were not pheresed (21, 75%) were deemed as failure for this strategy. The patient population included 14 males and 14 females with NHL (15), MM (6), AML (3) (AML no longer eligible due to possible leukemia mobilization), HD (3) and DSRCT (1), ages 17-76. Patients were remobilized with GCSF (10ug/kg/day SQ) on days 1-4 plus AMD3100 day 4 (240ug/kg/day SQ) and continued until goal reached. Apheresis began on day 5 and continued for a maximum of 7 days. The average PB CD34/uL for the failed mobilization was 6.1 and for AMD3100 was 24.7. The average fold increase per patient ranged from 0.86 to 147 (median 4.2-7.5). There was an average of 4.4 E6 CD34/kg cells collected by all patients (3.9 for those failing GCSF alone and 4.8 for those failing chemomobilization). 86 % of patients collected ≥ 2 E6 CD34/kg. 70 % of patients collected ≥ 4 E6/kg and 71 % of patients collected ≥ 2 E6/kg cells in 1 or 2 days of apheresis. The median number of days to collect ≥ 2 E6 was 4 overall, 4 NHL, 2 HD, 3.5 AML and 6 for MM patients (3 underwent planned tandem transplant requiring 4 E6 cells). The average number of days to collect > 2 E6 was 3.96 (range 1-7) and to collect > 4 was 2.9 (range 1-6). No serious adverse events occurred during mobilization. 24/28 patients received a transplant. The average number of days to ANC recovery was 10.6 and to platelet engraftment, 17.1. 5 patients died before 6 months post transplant with 14 patients alive and well. The combination of AMD3100 and GCSF appears to be effective in mobilizing optimal numbers of CD34+ cells in patients failing prior chemotherapy or growth factor stem cell mobilization. This represents the largest single institution experience using AMD3100 in a salvage setting. Our results compare favorably with previously reported outcomes with AMD3100 in multicenter use and against historical results with repeated chemotherapy or growth factor mobilization, due perhaps in part to a relatively consistent definition of mobilization failure and early intervention with this salvage agent. Our results support the efficacy and safety of the early use of AMD3100 in patients failing to mobilize or collect sufficient stem cells for PBSCT.

Comparison of Successful Collections in Multi-Center Study with Collections at VCU

AMD3100 compassionate use protocol patients (115)				VCU patients (28)		
Disease	Overall successful collection	failed mobilization Cytokine	chemotherapy + GCSF	Overall % successful collection	failed mobilization G-CSF (11)	chemotherapy + G-CSF (16)
NHL	63	53	71	87	60	100
MM	71	75	68	83	80	100
HD	76	75	78	100	100	100

in VCU study successful collection defined as ≥ 2E6 CD34/kg

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HEMATOPOIETIC STEM CELL TRANSPLANTATION WITH AUTOLOGOUS CORD BLOOD UNITS IN TWO PATIENTS WITH SEVERE APLASTIC ANEMIA: TIME FOR REASSESSMENT?

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Umbilical cord blood units (CBU), which contain a large number of hematopoietic stem cells (HSC), have been used successfully for allogeneic transplantation to treat a variety of benign and malignant hematologic disorders as well as genetic inborn errors of metabolism. It is now considered an acceptable alternative source for HSC when autologous or HLA-identical HSC are unavailable. This advance has resulted in the establishment of not-for-profit and for-profit cord blood banking banks for autologous and allogeneic transplantation. There is a wide consensus against private banking of autologous CBUs for the following reasons: 1) families may be vulnerable to emotional marketing at the time of birth of a child; 2) the life-time likelihood of using autologous HSC transplant is low, between1/10,000-1/200,000; 3) empirical evidence that children will need their own cord blood for future use is lacking; 4) no evidence of the safety or effectiveness of autologous CBU transplantation for the treatment of malignant diseases. Two patients (5 yr old girl and a 9 yr old girl) were diagnosed with idiopatic severe aplastic anemia (SAA). Both underwent successful immunosuppressive and myeloablative treatment followed by HSC transplantation from autologous CBUs. In one patient (5 yr old girl) this was the first line of therapy, and in the second (9 yr old girl) it was offered after failure of a course of standard immunosuppressive therapy. The conditioning therapy consisted of cyclophosphamide and rabbit ATG . There were no severe transplant-related adverse effects. Myeloid engraftment occurred on days +17 and +21 post-transplant, respectively. Platelet engraftment of $>20{,}000/mm^3$ occurred on days +20 and +31, and $>50{,}000/mm^3$ on days +36 and +42, respectively. At 8 months and 3 months post-transplant both patients have normal peripheral counts and do not require further immunosuppressive therapy. Both had successfully re-integrated into the school system. The rapid and uneventful recovery suggests a favorable role for a short course of immunosuppressive therapy and HSC transplant from an autologous CBU. This may re-open the discussion regarding the value of cryopreservation of large number of CBUs.